Provisional ACIP Recommendations for Postexposure Prophylaxis of Severe Varicella during a Varicella Zoster Immune Globulin Shortage

The ACIP was informed by the only U.S.-licensed manufacturer of varicella zoster immune globulin (VZIG) (Massachusetts Public Health Biologic Laboratories, Boston, MA) that it had discontinued production of VZIG. The limited supplies of 625 U vials of VZIG from the sole authorized distributor, FFF Enterprises (Temecula, CA), are expected to last until early 2006. The U.S. Food and Drug Administration is encouraging manufacturers to submit Investigational New Drug applications for VZIG products, with the goal of licensing a new product (http://www.fda.gov/cber/infosheets/mphvzig092005.htm).

In October 2005, the ACIP approved the following recommendations for postexposure prophylaxis of severe varicella infection during a VZIG shortage.

For postexposure prophylaxis of varicella of patients without evidence of immunity (without history of disease or have never been vaccinated, http://www.cdc.gov/nip/vaccine/varicella/varicella_acip_recs.pdf) who are at high risk for severe disease and complications, VZIG is the preferred method. VZIG can be ordered from the sole authorized US distributor, FFF Enterprises (Temecula, CA) at 1-800-843-7477 or via the Internet at www.fffenterprises.com. FFF Enterprises delivers VZIG on an as needed basis (i.e., when there is an identified exposed person for whom VZIG is indicated). Indications, administration, and dosage of VZIG were stated in the 1996 ACIP recommendations for prevention of varicella (MMWR 1996;45:20-24; http://www.cdc.gov/mmwr/preview/mmwrhtml/00042990.htm). However, in 1999, postexposure use of varicella vaccine was recommended for healthy persons, offering an alternate postexposure prophylaxis method for healthy adolescents and adults (http://www.cdc.gov/mmwr/PDF/rr/rr4806.pdf). The vaccine should be administered within 3 days (and up to 5 days) postexposure. If illness occurs, with or without postexposure vaccination, antiviral treatment (e.g., acyclovir) is recommended for adolescents and adults.

If VZIG is not available, intravenous immune globulin (IGIV) can be used[1]. The recommendation for use of IGIV is based on "best judgment of experts" and is supported by reports comparing VZV IgG antibody titers measured in both IGIV and VZIG preparations and patients given IGIV and VZIG. Licensed IGIV preparations contain anti-varicella antibodies at varying levels. No clinical data demonstrating effectiveness of IGIV for postexposure prophylaxis of varicella are available.

Indications for use of IGIV*

1. Immunocompromised patients.
2. Neonates whose mothers develop signs and symptoms of varicella around the time of delivery (5 days before to 2 days after).

[1] Another method indicated by some experts for postexposure prophylaxis of varicella is acyclovir. Limited data on acyclovir as postexposure prophylaxis are available for healthy children only, no studies were done for adults. However, limited clinical experience supports use of acyclovir as postexposure prophylaxis and clinicians may choose this option, with or without other methods. If acyclovir is used as postexposure prohlylaxis, the recommendation is for administration beginning from day 7 to day 10 after exposure for a total of 7 days of therapy. The recommended dose is 40-80 mg/kg/day divided into 4 doses (children) and 800 mg 4 times/day (adults). If illness occurs, antiviral therapy should be instituted at the earliest signs or symptoms. If the patient did not develop disease, varicella vaccine should be administered at a later date if it is not contraindicated.

3. Premature infants exposed during the neonatal period whose mothers do not have evidence of immunity.
4. Premature infants who are <28 weeks of gestation or who weigh ≤1,000 g at birth, exposed during the neonatal period, regardless of maternal history of varicella.
5. Pregnant women: Clinicians may choose either to administer IGIV or closely monitor the pregnant woman for signs and symptoms of varicella and institute treatment with acyclovir if illness develops.

* Note: A new dose of IGIV may not be necessary if a patient is receiving IGIV therapy at a dose of 400 mg/kg or greater at regular intervals and if the last dose was administered within 3 weeks of exposure to varicella.

Administration
Based on experience with VZIG, IGIV could be expected to provide maximum benefit when administered as soon as possible after exposure and may be effective if administered as late as 96 hours after exposure. IGIV should be administered intravenously as directed by the manufacturer.

Dosage
The recommended IGIV dose for postexposure prophylaxis of varicella is 400 mg/kg administered once. This dose is estimated to yield VZV antibody titers in the recipients comparable to titers produced by the recommended VZIG dose (22.5 mg/kg).

Interval between administration of IGIV and varicella vaccine
Any patient to whom IGIV is administered to prevent varicella, should subsequently receive varicella vaccine provided the vaccine is not contraindicated. Varicella vaccination should be delayed until 8 months following IGIV administration. Varicella vaccine is not needed if the patient develops varicella after administration of IGIV.

Antiviral therapy
Any patient who received IGIV should be observed closely for signs or symptoms of varicella for 28 days following exposure (IGIV, similar to VZIG, may prolong the incubation period by ≥1 week) and antiviral therapy should be instituted immediately if signs or symptoms of varicella disease occur.

The route and duration of therapy should be determined by specific host factors, extent of infection, and initial response to therapy.